REMARKS

Status of the Claims

Claims 1-25 were rejected. Claims 12-18, 20 and 21 have been canceled without prejudice or disclaimer. Applicant reserves the right to pursue subject matter of claims 12-18, 20 and 21 in a continuation or divisional application. Claims 1-11, 19, and 22-25 are pending.

Claims 1, 2, 3, 11, 19, 22, and 24 have been amended. To expedite prosecution, claim 1 has been amended without prejudice or disclaimer to delete the subject matter drawn to a complement of the nucleic acid sequences of (a) through (d). Applicant reserves the right to pursue deleted subject matter of claim 1 in a continuation or divisional application. Claims 2, 3, 11, 19, 22 and 24 have been amended to more clearly define the scope of the invention. No new matter has been entered by way of these amendments.

The Objection to the Claims Should Be Withdrawn

The Examiner has objected to Claim 11 for improper article usage. Claim 11 has been amended to recite "*the* plant" and is, therefore, in proper format. Claim 2 was objected to for failing to limit the subject matter of a previous claim from which it depends. Claim 2 has been amended to recite "*the* isolated" and, as such, properly limits the scope of claim 2. Accordingly, it is respectfully requested that the objection to claims 2 and 11 be withdrawn.

The Rejections Under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn

Enablement

The Examiner rejected claims 1-11, 19 and 22-25 under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable one skilled in the art to make or use the invention. This rejection is respectfully traversed.

The Examiner asserts that the specification, while enabling for nucleic acids encoding SEQ ID NO:3 or 5, host cells, plants, plant cells and seeds comprising them, and method of using them to make SEQ ID NO:3 or 5, does not reasonably provide enablement for methods and compositions drawn to nucleic acids encoding pesticidal protein with 95% sequence identity to

SEQ ID NO:3 or 5, nucleic acids with 95% identity to SEQ ID NO:1, 2, or 4, or a complement of those nucleic acids, host cells, plants, plant cells and seeds comprising them, and method of using them to make a pesticidal protein with 95% identity to SEQ ID NO:1, 2 or 4. The Examiner states that the specification fails to provide guidance for which amino acids of SEQ ID NO:3 or 5 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain the activity of the encoded protein, as well as which regions of the protein can tolerate insertions and still produce a functional protein. It is noted that the Examiner has made no reference to the enablement of the nucleotide sequence set forth in SEQ ID NO:6, nucleotide sequences with 95% identity to SEQ ID NO:6, a nucleotide sequence encoding SEQ ID NO:7, nor a nucleotide sequence encoding a polypeptide with 95% identity to SEQ ID NO:7.

The Examiner appears to be suggesting that in order to satisfy the enablement requirement Applicants must demonstrate that every pesticidal polypeptide and variant and fragment thereof encompassed by the claims could be used to successfully practice the invention, such that no experimentation would be required. According to the applicable case law, however, the test of enablement is not whether experimentation is necessary to make and use an invention, but rather if experimentation is necessary, whether it is undue. *In re Angstadt*, 198 USPQ 214, 219 (C.C.P.A. 1976). Furthermore, a considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

The test of whether an invention requires undue experimentation is not based on a single factor, but rather is a conclusion reached by weighing many factors. *Id.* at 1404. Factors to be considered in determining whether undue experimentation is required include the quantity of experimentation necessary, the amount of guidance provided in the specification, the presence of working examples of the invention in the application, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability in the art, and the breadth of the claimed invention. *Id.* Accordingly, the holding of *Wands* does not require that Applicants provide as working examples every pesticidal polypeptide that could be used to practice the present invention. Rather, *Wands* sets out factors to be considered in determining whether undue experimentation is required to make and use the invention.

The Examiner argues that the specification does not enable one of skill in the art to make and use nucleic acids that encode polypeptides that retain pesticidal activity and have at least 95% sequence identity to SEQ ID NO:1, 2, or 4, or 95% sequence identity to a nucleotide sequence that encodes SEQ ID NO:3 or 5. The Examiner incorrectly bases this conclusion solely on the number of possible nucleic acids having the recited percent identity to SEQ ID NO:1, 2 or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5 while ignoring the other factors set forth in *Wands* for assessing whether undue experimentation is required. In particular, the Examiner has improperly discounted the guidance provided in the specification and the working examples set forth in the application (page 4 of the Office Action mailed February 14, 2006).

First, sufficient guidance for making and using the recited sequences is present in the specification. The claimed variants and fragments of SEQ ID NO:1, 2, 4, or 6, or nucleotide sequences encoding SEQ ID NO:3, 5, or 7 are limited by a percent identity (i.e., 95% identity) and further limited by the functional requirement that they possess pesticidal activity. Guidance for preparing variants and fragments of SEQ ID NO:1, 2, 4, or 6, or nucleotide sequences encoding SEQ ID NO:3, 5, or 7 and for determining percent identity is provided in the specification and generally known in the art. See page 9, lines 23-29, and pages 10-15. Numerous delta-endotoxins were also well known in the art at the time the application was filed. See Crickmore *et al.* (1998) *Microbiol. Molec. Biol. Rev.* 62:807-813, which is incorporated by reference on page 2, lines 8-9 and is submitted herewith as Appendix A, and Crickmore *et al.* (2004) *Bacillus thuringiensis Toxin Nomenclature* at lifesci.sussex.ac.uk/Home/Neil_Crickmore/Bt. The necessary molecular biology and mutagenesis techniques for preparing the variants and fragments of pesticidal sequences of the invention are routine. Moreover, methods for assessing the pesticidal activity of a polypeptide are readily available in the art and provided in the specification. See, for example, page 12, lines 24-28 and Examples 8, 9, and 11.

In order to identify the pesticidal sequences encompassed by the present claims, one of skill in the art would only need to prepare variants and fragments of the nucleotide sequence of SEQ ID NO:1, 2, 4, or 6, or a nucleotide sequence encoding SEQ ID NO:3, 5, or 7, having the specified characteristics recited in the claims (e.g., at least 95% identity) and then assay these

polypeptides for pesticidal activity. Routine methods for preparing variants and fragments and testing the resulting polypeptides for pesticidal activity are routine in the art and described in the specification. Although some experimentation is required to practice the claimed invention, it is now customary in the art to generate a large number of sequences and to test them in a large-scale assay for a desired function, and, therefore, such experimentation is not undue, particularly in view of the routine nature of the required methods. Contrary to the Examiner's conclusions, in order to identify variants and fragments of the nucleotide sequence of SEQ ID NO:1, 2, 4, or 6, or a nucleotide sequence encoding SEQ ID NO:3, 5, or 7 that could be used in the invention, a person skilled in the art would only need to utilize standard molecular biology and mutagenesis techniques and routine screening tests for pesticidal activity. Therefore, given the level of skill and knowledge in the art, the availability of standard methods and assays, and the significant guidance provided in the specification, Applicants respectfully submit that the amount of experimentation required to identify delta-endotoxins and variants and fragments thereof having pesticidal activity and the structural features recited in the claims is routine, not undue.

The Examiner further argues that mutation of sequences, even conservative substitutions, does not produce predictable results and, therefore, the specification is not enabling with respect to variants of the nucleotide sequence of SEQ ID NO:1, 2, or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5. The Office Action cites Lazar *et al.* (1988) *Molecular and Cellular Biology* 8:1247-1252 and Hill *et al.* (1998) *Biochem. Biophys. Res. Comm.* 244:573-577 in support of the general unpredictability of the art with respect to modification of nucleotide sequences. Each reference, however, simply teaches that alteration of highly conserved sequences will disrupt function. Lazar *et al.* teach that alterations in amino acid residues 47 and 48 in TGF-alpha can alter the activity of the polypeptide. Contrary to the Examiner's conclusion, the alteration in the polypeptide was specifically designed to occur at amino acid positions that are highly conserved in the EGF-like family of polypeptides. Similarly, the modified residues described by Hill *et al.* were conserved among bacterial and plant ADP-glucose pyrophosphorylases. As set forth in the first line of the abstract, "[t]wo *absolutely conserved* histidines and a third *highly conserved* histidine are noted in eleven bacterial and plant ADP-glucose pyrophosphorylases" (emphasis added). These absolutely and highly conserved

histidines were mutagenized and characterized in the paper. One of skill in the art would not be surprised that modification of one of these highly conserved amino acids would lead to the loss of function described by the authors. Applicants further note that the Lazar *et al.* and the Hill *et al.* references are directed to TGF-alpha and ADP-glucose pyrophosphorylase, neither of which has any relation to the pesticidal sequences of the present invention. Thus, the cited references do not support the Examiner's broad assertion of inherent unpredictability of protein function resulting from the mutation of the underlying nucleotide sequence. In fact, both references support Applicants' arguments that at the time the application was filed one of skill in the art could modify polypeptide sequences and test the resulting variants for biological activity.

Furthermore, the specification provides guidance regarding conservative modifications that are unlikely to disrupt biological activity. See, for example, pages 12-14. Thus, by reference to a standard codon table, one of skill in the art could predict which modifications would not affect the biological activity of the encoded polypeptide. Also, the specification lists numerous examples of conserved residues that are not likely to tolerate substitution (see page 14), delineates conserved domains characteristic of delta-endotoxin proteins (see page 4), and highlights conserved residues in the sequences of the invention (see Figure 1 as originally filed). The replacement figure does not highlight conserved residues, however, one of skill in the art would understand how to use the alignment provided in the replacement figure to identify conserved residues using, for example, the methods described in the instant specification (see pages 10-11).

Moreover, as described above, Applicants have disclosed pesticidal sequences, and variants and fragments thereof, and the art was replete with additional delta-endotoxin sequences at the time the application was filed. Information relating to conserved regions of delta-endotoxins may be obtained from these sequences. A person of skill in the art would appreciate that comparison and alignment of known delta-endotoxin sequences may reveal information regarding appropriate sites or regions for modifications. By aligning these sequences, one may be able to identify conserved residues or regions within these proteins that are unlikely to tolerate mutation and still retain pesticidal activity. Methods for aligning sequences, such as by using the CLUSTAL algorithm, are described in the specification. See pages 9-11.

In addition, detailed information about the structure of delta-endotoxins was known in the art. See, for example, Li *et al.* (1991) *Nature* 353:815-821 (describing the crystal structure of the Cry3A protein), which is incorporated by reference on page 12 of the specification, and Morse *et al.* (2001) *Structure* 9:409-417, both of which are submitted herewith (Appendices B and C, respectively). Delta-endotoxins are extremely well-characterized and related to each other to various degrees by similarities in their amino acid sequences and tertiary structures. A combined consideration of the published structural analyses of delta-endotoxins and the reported functions associated with particular structures, motifs, and the like indicates that specific regions of the toxin are correlated with particular functions and discrete steps of the mode of action of the protein. Thus, a rational scheme for determining the regions of a delta-endotoxin that would tolerate modification is provided. Based on the regions of delta-endotoxins that are conserved among protein family members, the skilled artisan could choose among possible modifications to produce polypeptides within the structural parameters set forth in the claims and then test these modified variants to determine if they retain pesticidal activity. In light of the guidance provided in the specification and the state of the art with respect to delta-endotoxins, a skilled artisan could readily conclude which amino acids are essential for structure and function and could envisage similar sequences that are 95% identical to the nucleotide sequence of SEQ ID NO:1, 2, 4, or 6, or a nucleotide sequence encoding SEQ ID NO:3, 5, or 7, and that retain pesticidal activity. As such, one of skill in the art could identify the pesticidal sequences encompassed by the present claims without undue experimentation.

The Examiner has also cited Guo *et al.* (2004) *Proc. Natl. Acad. Sci. USA* 101:9205-9210 for the proposition that increasing the number of amino acid substitutions in a protein increases the probability that the protein will be functionally inactivated. The Examiner uses this reference as evidence that making and analyzing delta-endotoxins that have multiple amino acid substitutions but that still retain pesticidal activity will require undue experimentation. The Examiner, however, has mischaracterized the Guo *et al.* reference. The cited reference is directed to analysis of the probability that a *random* amino acid replacement will lead to a protein's functional inactivation (emphasis added). In contrast, the specification provides a rational and systematic method for designing delta-endotoxin variants that retain pesticidal

activity. One of skill in the art would appreciate that regions known to be important for pesticidal activity would be unlikely to tolerate significant mutation and, therefore, would not expect such mutations to result in a biologically active protein. Thus, the teachings of Guo *et al.* do not support the Examiner's conclusion that the present claims lack enablement.

The Examiner further relies on the teachings of de Maagd *et al.* (1999) *Appl. Environ. Microbiol.* 65:4369-4374, Tounsi *et al.* (2003) *J. Appl. Microbiol.* 95:23-28 and Angsuthanasombat *et al.* (2001) *J. Biochem. Mol. Biol.* 34:402-407 in support of the assertion that amino acid substitutions in delta-endotoxin proteins are unpredictable. However, each of these references describes substitutions (which are largely non-conservative) in *conserved* regions. de Maagd *et al.* teaches that the insertion of several groups of amino acids within Domain III of Cry1E with the corresponding amino acids of Cry1C will alter the specificity and/or toxicity of Cry1E. Since the conserved Domain III is well known by those of skill in the art to be involved in specificity of a delta-endotoxin toward a pest, it would be no surprise that alteration of this domain could affect specificity of the protein. In fact, that was the intention of de Maagd *et al.* Similarly, Tounsi *et al.* discuss the single amino acid difference between Cry1Ia1 and Cry1Ia2 (which is a non-conservative substitution of aspartic acid for tyrosine at position 233) as being critical to insecticidal specificity of these two toxins. Again, this substitution occurs in the conserved Domain I. Finally, Angsuthanasombat *et al.* teach a critical amino acid residue at position 136 where even a conservative substitution could lead to loss of pesticidal activity. Yet again, the authors specifically targeted amino acids in conserved Domain I in order to alter function. Since the instant specification clearly defines the conserved domains described by the aforementioned references with respect to the claimed sequences (see page 4), one of skill in the art would appreciate that substitutions made in these domains could lead to a loss of specificity and/or toxicity. Further, the references cited by the Examiner actually support the Applicant's assertion that one of skill in the art at the time of the invention would understand which residues could be altered to *change* the function of delta-endotoxins, implying that one of skill would equally understand which residues *not* to change when maintenance of function is desired.

In establishing non-enablement, the burden rests initially with the Examiner to substantiate the unpredictability of the art and that, given the unpredictability, the specification does not provide sufficient information to guide those of skill to make and use the claimed invention across the full scope of the claims. In view of the discussion above, the references cited by the Examiner fails to support the position that claims 1-11, 19, and 22-25 are not enabled.

The Examiner also states that the specification fails to teach how to use a complement of nucleic acids encoding pesticidal protein with 95% identity to SEQ ID NO:3 or 5 or nucleic acids with 95% identity to SEQ ID NO:1, 2, or 4. The Applicant respectfully disagrees. Page 9, lines 2-5 state that the complement of a claimed nucleotide sequence is one that would hybridize to a given nucleotide sequence to thereby form a stable duplex. Page 15, lines 3-8 state that hybridization methods (using, for example, complementary sequences) can be used to screen cDNA or genomic libraries for delta-endotoxin sequences having substantial identity to the sequences of the invention. Therefore, the specification clearly teaches how to use the complement of a nucleic acid sequence of the invention to, for example, screen for similar delta-endotoxin sequences. However, to expedite prosecution, claim 1 has been amended to delete the subject matter pertaining to complementary sequences.

The Examiner further maintains that the specification does not enable the transformation of any plant with a nucleotide sequence with 95% identity to the nucleotide sequence of SEQ ID NO:1, 2, or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5 because undue trial and error experimentation would be required to screen for nucleotide sequences encompassed by the claims and plants transformed therewith to identify those plants with pesticidal activity. As discussed above, the amount of experimentation required to identify a nucleotide sequence that has 95% sequence identity to SEQ ID NO:1, 2, 4, or 6, or to a nucleotide sequence encoding SEQ ID NO:3, 5, or 7 is not undue. With respect to transformation of plants with these sequences, the specification provides routine methods for transformation of plants with nucleotide sequences and the regeneration of transgenic plants. See pages 22-28 and Examples 13 and 14. Given the guidance provided in the specification and the knowledge in the art, the

claims directed to transformation of a plant with a delta-endotoxin sequence, or variant or fragment thereof, are fully enabled.

In light of the above arguments, the level of skill and knowledge in the art, and the guidance provided in the specification, Applicants respectfully submit that the specification is enabling for the full scope of claims 1-11, 19, and 22-25. Thus, the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement should be withdrawn.

Written Description

Claims 1-11, 19, and 22-25 were further rejected under 35 U.S.C. § 112, first paragraph, as failing to satisfy the written description requirement. The rejection is respectfully traversed.

The Examiner asserts that the disclosure is insufficient to support claims that are drawn to a genus of nucleic acids having 95% sequence identity to SEQ ID NO:1, 2, or 4, or nucleic acids encoding polypeptides having 95% identity to SEQ ID NO:3 or 5. The Applicant again notes that the Examiner has made no reference to the written description of the nucleotide sequence set forth in SEQ ID NO:6, nucleotide sequences with 95% identity to SEQ ID NO:6, a nucleotide sequence encoding SEQ ID NO:7, nor a nucleotide sequence encoding a polypeptide with 95% identity to SEQ ID NO:7.

In order to satisfy the written description requirement of 35 U.S.C. § 112, the application must reasonably convey to one skilled in the art that the applicant was in possession of the claimed subject matter at the time the application was filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). Every species encompassed by the claimed invention, however, need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. *Utter v. Hiraga*, 845 F.2d 993, 6 USPQ2d 1709 (Fed. Cir. 1988). The Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P. v. Faulding In.*, 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the limitations at issue in the claims.").

Moreover, the "Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, ¶ 1, 'Written Description' Requirement" state that a genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics , *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. This is in accordance with the standard for written description set forth in *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing *Fiers v. Revel* 984 F.2d 1164 (Fed. Cir. 1993). In *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.2d 926 (Fed. Cir. 2002), the Federal Circuit adopted the PTO standard for written description, stating:

> [U]nder the Guidelines, the written description requirement would be met . . . if the functional characteristics of [a genus of polypeptides] were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed. We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement."

The claims of the present application meet the requirements for written description set forth by the Federal Circuit. The claims recite that the nucleic acid have 95% sequence identity to the nucleotide sequence of SEQ ID NO:1, 2, 4, or 6, or to a nucleotide sequence encoding SEQ ID NO:3, 5, or 7. Methods for determining percent identity between any two sequences are known in the art and are provided in the specification. See pages 9-15. As discussed above, nucleotide sequences for full-length AXMI-008 (SEQ ID NO:1), as well as variants and fragments (e.g., SEQ ID NO:2, 4 and 6) are disclosed in the specification. Numerous delta-endotoxin sequences were also generally known in the art at the time the application was filed. Moreover, detailed information regarding the structure of delta-endotoxins and the reported functions associated with particular structures, regions, and motifs was also available in the prior art as well as discussed in detail on page 2, lines 22-29, Figure legend 1, and on pages 14. At the time of filing, it was known that delta-endotoxins generally comprise three domains, a seven-

helix bundle that is involved in pore formation, a three-sheet domain that has been implicated in pore formation, and a beta-sandwich motif. See Li *et al.* (1991) *Nature* 305:815-821. Thus, the recitation of polypeptides having a particular percent identity to a delta-endotoxin provides very specific and defined structural parameters of the sequences that can be used in the invention. These structural limitations are sufficient to distinguish the nucleotide and amino acid sequences of the invention from other nucleic acids and polypeptides and thus sufficiently define the genus of sequences useful in the practice of the present invention.

The Examiner is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Here, Applicants have provided nucleotide and amino acid sequences for exemplary pesticidal sequences and variants and fragments thereof encompassed by the claims. Moreover, numerous delta-endotoxin sequences were known and readily available in the art. Therefore, Applicants submit that in view of the present disclosure and the knowledge and level of skill in the art the skilled artisan would envision the claimed invention.

The description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of polypeptides may therefore be described by means of a recitation of a representative number of amino acid sequences that fall within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). The recitation of a predictable structure (i.e., an amino acid sequence having a specified percent identity or number of contiguous amino acid residues of a particular sequence) is sufficient to satisfy the written

description requirement. Thus, the application provides the structural features that characterize sequences having at least 95% sequence identity to SEQ ID NO:1, 2, 4, or 6, or to a nucleotide sequence encoding SEQ ID NO:3, 5, or 7 that retain pesticidal activity.

An Applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the sequences recited in the claims. *Id.*, citing *Lilly* at 1568. The present claims further recite functional characteristics that distinguish the sequences of the claimed genus. Specifically, the claims recite that the sequences having at least 95% sequence identity to SEQ ID NO:1, 2, 4, or 6, or to a nucleotide sequence encoding SEQ ID NO:3, 5, or 7 encode proteins which have pesticidal activity. The specification and the art provide standard assays that may be used to measure pesticidal activity. See, for example, page 8, lines 27-31. Furthermore, as noted above, Applicants have disclosed fragment sequences that retain pesticidal activity (e.g., SEQ ID NO:4, which encodes a fragment of SEQ ID NO:3, and SEQ ID NO:6, which encodes a fragment of SEQ ID NO:1). Accordingly, both the structural and functional properties that characterize the genus of sequences that can be used to practice the invention are specifically recited in the claims. The sequences that fall within the scope of the claims can readily be identified by the methods set forth in the specification.

In summary, the specification provides an adequate written description of the claimed invention. In particular, the specification provides: nucleotide and amino acid sequences for pesticidal toxins, and variants and fragments thereof, that fall within the scope of the claims; guidance regarding sequence alterations that do not disrupt pesticidal activity of a toxin; guidance for determining percent identity; and methods for assaying the pesticidal activity of proteins. In view of the above remarks and claim amendments, Applicants submit that the relevant identifying structural and functional properties of the genus of sequences of the present invention would be clearly recognized by one of skill in the art. Consequently, Applicants were in possession of the invention at the time the application was filed, and the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of written description should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph Should Be Withdrawn

Claims 3, 11, and 19, as well as dependent claims therefrom, were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Claim 3 has been amended to recite "relative to the GC content of SEQ ID NO:1, 2, or 4." Support for this amendment can be found on page 27, lines 1-3. Claim 11 has been amended to recite "*the* plant" of claim 9. Claim 9 depends depends from claim 8, which depends from claim 6, which depends from claim 4, which depends from claim 1. Therefore, as amended, claim 11 now describes a transgenic seed derived from a plant that comprises a host cell that contains a vector comprising the nucleic acid of claim 1. Claim 19 has been amended to recite "*the* nucleic acid molecule" such that claim 19 now encompasses a method for producing a polypeptide by culturing a host cell that contains a vector that comprises the nucleic acid of claim 1. Accordingly, the rejection of claims 3, 11, and 19 under 35 U.S.C. § 112, second paragraph should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 22 and 24 were rejected under 35 U.S.C. § 102(b) as being anticipated by Barton *et al.* (U.S. Patent No. 6,833,449). Barton *et al.* teach tobacco plants transformed with a nucleic acid encoding a CryI protein. The Examiner states that the recitation of "a" before "nucleotide sequence of SEQ ID NO:1, 2 or 4" in parts (a) and (d) and "an" before "amino acid sequence of SEQ ID NO:3, 5, or 7" in part (c) encompasses nucleic acids that comprise the full-length sequence of SEQ ID NO:1, 2 or 4, or any portion of SEQ ID NO:1, 2 or 4 or that encode the full-length of SEQ ID NO:3, 5, or 7 or any portion of SEQ ID NO:3, 5, or 7. Claims 22 and 24 have been amended to recite "the" before "nucleotide sequence" and "amino acid sequence." As such, the CryI protein taught in Barton *et al.* does not comprise the sequence of SEQ ID NO:1, 2, 4, or 6, nor a sequence with 95% identity to SEQ ID NO:1, 2, 4, or 6. Accordingly, the rejection of claims 22 and 24 under 35 U.S.C. § 102(b) should be withdrawn.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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